

**REMARKS**

In response to the Final Office Action dated July 24, 2007, Applicants filed an Amendment and Response along with a Notice of Appeal on January 24, 2008. As indicated in the Advisory Action dated February 28, 2008, the foregoing Amendment and Response was not entered. Accordingly, Applicants file herewith a Request for Continued Examination and the present Amendment and respectfully request that the present Amendment be entered.

Claims 13-16 and 26-32 were pending in the application. Claim 13 has been amended and claim 32 has been canceled. Accordingly, upon entry of the amendments presented herein, claims 13-16 and 26-31 will remain pending in the application.

Claim 13 has been amended to specify “a gluten sensitive enteropathic autoimmune disease” and the step of correlating significantly increased amounts of the IgA antibodies as compared to a control sample with a diagnosis of a gluten sensitive enteropathic autoimmune disease. Support for this amendment can be found throughout the specification and claims as originally filed. Specifically, support is available at page 2, line 29 through page 3, line 6; page 11 (lines 7-20); page 14 (lines 10-22); and page 22 (lines 4-17).

Claims 15-16 and 26-31 have been withdrawn. However, as acknowledged by the Examiner, Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. It is further Applicants’ understanding that the species election was for search purposes only and that the search will be extended to additional species upon a finding of allowable subject matter.

The foregoing amendments should in no way be construed as an acquiescence to any of the Examiner's rejections, and have been made solely to expedite examination of the present application and to place the pending claims in better condition for allowance. Accordingly, Applicants respectfully request that the foregoing claim amendments be entered. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s). *No new matter has been added.*

***Acknowledgment of the Examiner's Withdrawal of Certain Rejections and Objections***

In the present Office Action, the Examiner did not specifically acknowledge withdrawal of the following rejections and objections: (a) the prior objection to the specification as

improperly referencing the claims; (b) the prior objection to the specification as containing typographical errors; and (c) the prior rejection of claims 13 and 14 under 35 U.S.C. § 112, second paragraph as being indefinite. However, the foregoing objections and rejections are not raised in the present Office Action. Therefore, Applicants respectfully assume that these rejections have been withdrawn, and would appreciate confirmation of such by the Examiner.

***Rejection of Claim 32 Under 35 U.S.C. § 112, First Paragraph – Written Description***

The Examiner has rejected claim 32 as allegedly lacking written description under 35 U.S.C. § 112, First Paragraph. Specifically, the Examiner is of the opinion that “the specification does not disclose the diagnosis of a second autoimmune disease as currently recited” and that “[t]here is no description in the specification [of] diagnosing a second autoimmune disease as recited.”

Applicants respectfully traverse this rejection. However, to expedite prosecution and allowance of the pending claims, Applicants have canceled claim 32, thereby rendering this rejection moot. Accordingly, Applicants respectfully request that the Examiner withdraw the foregoing rejection.

***Rejection of Claims 13, 14 and 32 Under 35 U.S.C. § 112, First Paragraph - Enablement***

The Examiner has rejected claims 13, 14 and 32 under 35 U.S.C. § 112, First Paragraph, as lacking enablement because, according to the Examiner,

the specification, while being enabling for a method of diagnosing gluten sensitive enteropathy by testing a sample for IgA antibodies directed against human tissue transglutaminase and one other transglutaminase molecule selected from the group consisting of FXIIIA, TGk, TGx, TGe and Band 4.2 *and correlating significantly increased amounts of the IgA antibodies as compared to a control sample, with a diagnosis of gluten sensitive enteropathy*, does not reasonably provide enablement for the mere presence or decrease amounts of IgA antibodies for diagnosing gluten sensitive enteropathy (emphasis added).

Applicants respectfully traverse the foregoing rejection. However, to expedite prosecution and allowance of the pending claims, Applicants have canceled claim 32 and

amended claims 13 and 14 to specify the particular embodiment that the Examiner has deemed enabled.

Specifically, claim 13, as amended (and claims depending therefrom), is drawn to a method for diagnosing a gluten sensitive enteropathic autoimmune disease, comprising (a) taking a sample from a patient; (b) testing the sample for IgA antibodies against human tissue transglutaminase and at least one other transglutaminase molecule selected from the group consisting of a-subunit of factor XIII (FXIIIA), keratinocyte transglutaminase (TGk), transglutaminase X (TGx), epidermal transglutaminase (TGe) and Band 4.2; and (c) correlating significantly increased amounts of the IgA antibodies as compared to a control sample with a diagnosis of a gluten sensitive enteropathic autoimmune disease, thereby diagnosing a gluten sensitive enteropathic autoimmune disease. Further, as confirmed by the enclosed publications by Marietta *et al.*, *J Invest Dermatol.* 2008 Feb;128(2):332-5 (enclosed herewith as Appendix A) and Sardy *et al.*, *J Exp Med.* 2002 Mar 18;195(6):747 (enclosed herewith as Appendix B) it is clear that that the presently claimed methods can indeed be used for diagnosing a gluten sensitive enteropathic autoimmune disease, such as dermatitis herpetiformis.

In view of the foregoing, Applicants respectfully request that that the Examiner reconsider and withdraw the foregoing rejection.

***Rejection of Claim 32 Under 35 U.S.C. § 112, Second Paragraph***

The Examiner has rejected claim 32 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite because, according to the Examiner, “it is unclear if applicant is actually trying to diagnose two different diseases at the same time or if the applicant intends to somehow try and differentiate between the two diseases.”

Applicants respectfully traverse this rejection. However, as discussed above, Applicants have canceled claim 32, thereby rendering this rejection moot. Accordingly, Applicants respectfully request that the Examiner withdraw the foregoing rejection.

***Rejection of Claims 13 and 32 Under 35 U.S.C. § 102(b)***

The Examiner has rejected claims 13 and 32 under 35 U.S.C. § 102 as being anticipated by Schuppan *et al.* (US 6,319,726). The Examiner relies on Schuppan *et al.* for teaching “methods of detecting antibodies from body fluids by means of an immune reaction with tissue transglutaminase,” such as human tissue transglutaminase. The Examiner also relies on Schuppan *et al.* for teaching “that the tissue transglutaminase can be immobilized and used to detect antibodies in a sample for diagnosing celiac disease” and that such a method “is used to detect IgA antibodies.”

Applicants respectfully traverse this rejection. For a prior art reference to anticipate a claimed invention under 35 U.S.C. § 102, the prior art must teach *each* and *every* element of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987). The presently claimed methods for diagnosing a gluten sensitive enteropathic autoimmune disease, comprising taking a sample from a patient, *testing the sample for IgA antibodies against human tissue transglutaminase and at least one other transglutaminase molecule selected from the group consisting of a-subunit of factor XIII (FXIIIa), keratinocyte transglutaminase (TGk), transglutaminase X (TGx), epidermal transglutaminase (TGe) and Band 4.2; and correlating significantly increased amounts of the IgA antibodies as compared to a control sample with a diagnosis of a gluten sensitive enteropathic autoimmune disease.*

As previously made of record, the aim of the present invention is to determine whether an autoimmune disease is caused, in part, by an enteropathy caused by a type of gluten sensitivity. Applicants acknowledge that the etiologies of the autoimmune diseases recited by Applicants at, for example, page 2, Table 2 of Applicants’ specification, are not fully known and/or understood. However, it is the object of the invention to provide a method for determining the etiology of an autoimmune disease, so as to enable treatment of the disease. Accordingly, the methods of the present invention are useful for further testing a suspected or known autoimmune disease to provide a better means for diagnosis of the true nature and cause of the autoimmune disease under investigation.

In contrast, Schuppan *et al.* teach methods of *identifying coeliac disease/non-topical sprue disease* in a subject *by detecting the binding of antibodies* in body fluids to a target antigen (*i.e.*, tissue transglutaminase (tTG)) and *correlating the binding of said antibodies with the existence of coeliac disease* in the subject. Schuppan *et al.* fail to teach or suggest a diagnosing a *gluten sensitive enteropathic autoimmune disease* (*e.g.*, dermatitis herpetiformis, AI haemolytic anaemia, AI thrombocytopenic purpura, AI thyroid diseases, and atrophic gastritis – pernicious anaemia, Crohn’s disease, colitis ulcerosa, Goodpasture syndrome, IgA nephropathy or IgA glomerulonephritis, myasthenia gravis, partial lipodystrophy, polymyositis, primary biliary cirrhosis, primary sclerosing cholangitis, progressive systemic sclerosis, recurrent pericarditis, relapsing polychondritis, rheumatoid arthritis, rheumatism, sarcoidosis, Sjögren’s syndrome, SLE, splenic atrophy, type I (insulin-dependent) diabetes mellitus, diabetes mellitus of other types, Wegener granulomatosis, ulcerative colitis, vasculitis (both systemic and cutaneous), and vitiligo) comprising taking a sample from a patient, testing the sample for IgA antibodies against human tissue transglutaminase and *at least one other transglutaminase molecule selected from the group consisting of a-subunit of factor XIII (FXIIIa), keratinocyte transglutaminase (TGk), transglutaminase X (TGx), epidermal transglutaminase (TGe) and Band 4.2*; and *correlating significantly increased amounts of the IgA antibodies as compared to a control sample with a diagnosis of a gluten sensitive enteropathic autoimmune disease*. Since Schuppan *et al.* fail to teach or suggest each and every element of the present invention, *i.e.*, methods of diagnosing a *gluten sensitive enteropathic autoimmune disease* which encompasses the detection of antibodies against human tissue transglutaminase *and at least one other transglutaminase molecule selected from group consisting of FXIIIa, TGk, transglutaminase X TGx, TGe and Band 4.2* and *correlating significantly increased amounts of the IgA antibodies as compared to a control sample with a diagnosis of a gluten sensitive enteropathic autoimmune disease*, claim 13 is novel over the cited reference.

In view of the foregoing, Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

**CONCLUSION**

It is respectfully submitted that the entering of the Amendment would allow the Applicant to reply to the rejections raised in the Final Office Action (dated July 24, 2007) and the Advisory Action (dated February 28, 2008) and place the application in condition for allowance.

Should the Examiner feel that a telephone conference with Applicant's Attorney would expedite prosecution of the application and allowance of the claims, the Examiner is urged to contact the undersigned representative at (617) 227-7400.

Applicants submit herewith the requisite fee associated with the filing of this Amendment. However, should any additional fee be due, please charge such fee to our Deposit Account No. 12-0080, under Order No. HLZ-001USRCE, from which the undersigned is authorized to draw.

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Respectfully submitted,



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